REPORT DOCUMENTATION PAGE

Form Approved
OMB NO. 0704-0188

1. AGENCY USE ONLY (Leave Blank)	2. REPORT DATE 5/23/07	3. REPORT TYPE AND DATES COVERED Fiinal, 09/02/03 TO 123/31/06

4. TITLE AND SUBTITLE Toward High-Performance Neural Control of Prosthetic Devices	5. FUNDING NUMBERS N00014-03-1-0976
6. AUTHOR(S) Krishna Shenoy	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Stanford University 651 Serra Street Stanford, CA 94305	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) Office of Naval Research Ballston Centre Tower One 800 North Quincy Street Arlington, VA 22217-5660	10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

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12 a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited.	12 b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

See Attached

14. SUBJECT TERMS	15. NUMBER OF PAGES 11
	16. PRICE CODE

17. SECURITY CLASSIFICATION OR REPORT UNCLASSIFIED	18. SECURITY CLASSIFICATION ON THIS PAGE UNCLASSIFIED	19. SECURITY CLASSIFICATION OF ABSTRACT UNCLASSIFIED	20. LIMITATION OF ABSTRACT UL

NSN 7540-01-280-5500

Standard Form 298 (Rev.2-89)
Prescribed by ANSI Std. 239-18
298-102

FINAL TECHNICAL REPORT

21 May 2007

Project Title: Toward Neural Control of Prosthetic Devices
ONR Award No: N000140310976
Organization Award No: 123456789

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Scientific and Technical Objectives

Our scientific objective is to advance our fundamental understanding of how the brain plans and executes arm movements. Our technical objective is to design and build high-performance neural prostheses. Jointly, these objectives should provide a deeper understanding of the neural control of natural movement, and a better design of neural prostheses to restore movement to the disabled, including the disabled warfighter.

Approach

Our approach is twofold. First, we conduct basic systems neuroscience research using the techniques of chronic electrode-array electrophysiology (with non-human primates), computational neuroscience, theoretical neuroscience and behavior. This approach is employed in our basic neuroscience research. Second, to pursue our applied neural prosthesis research, we also "decode" neural activity in real-time and move computer cursors with these signals. This allows us to design and validate high-performance algorithms.

Concise Accomplishments

In the past three years (period of the award) we published on our basic science investigations concerning how movements are prepared. More specifically, we found that we could view neural activity as an attractor system wherein neural activity becomes more "accurate" as planning proceeds (Churchland et al. 2006). We also found that the speed of the upcoming arm movement, not just the direction and distance, is also planned (Churchland, Santhanam & Shenoy 2006). We also published an applied study demonstrating the design of an unprecedentedly fast and accurate neural prosthetic system (Santhanam et al. 2006). The importance of this result is that it is the first study to demonstrate that systems relying on implanted electrodes can substantially outperform (we report a factor of 4 increase) non-invasive (e.g., EEG) approaches or even other implanted-electrode approaches. Together, our basic and applied research has advanced the prospects of dramatically improving the quality of life of severely disabled patients, and amputees, including the warfighter.

Expanded Accomplishments

Recent progress in motor and communication prosthesis research has been fueled by recent discoveries in systems neuroscience, by the rapid advance of computational algorithms and circuit technologies, and by the advent of micro-electro-mechanical systems for interfacing with biological systems (bio-MEMS). However, significant barriers to continued progress exist, particularly when attempting to elucidate the design principles for dramatically higher performance neural prostheses. Thus we have focused our past and present research on lowering several of these barriers, which can be grouped into five major categories. Below we briefly review many of our recent and ongoing projects in these five areas. Taken together, this research has helped to (1) design and develop the massive new neuroengineering infrastructure necessary for cortical prosthetic systems, (2) establish the fundamental neural prosthetic behavioral paradigm wherein neural activity is processed in real time and fed back to the animal so as to enable real time control, and to begin to (3) apply non-linear dynamical systems modeling to multi-electrode cortical recordings in order to more deeply understand the underlying principles and mechanisms of primate cortical circuits

1) How does the brain prepare and generate arm movements?

Considerable systems neuroscience research has focused on the neural generation of arm movements, but relatively few investigations have focused on the preceding "planning" or "preparation" stage. We are investigating motor planning both because it is poorly understood scientifically, and because we suspect that it will provide the best source of fast and accurate prosthetic control signals.

In project 1 (P1) we discovered that disruption, via electrical microstimulation, of neural planning activity in dorsal premotor cortex (PMd) of rhesus monkeys increases movement reaction time (Churchland & Shenoy, *J Neurophysiology* 2007). This indicates that movement preparation is an actively-monitored process, and that movement can be delayed until inaccuracies are repaired. In P2 we discovered that action potential (spike) firing rates become computationally optimized during planning, approaching their ideal values over time (Churchland et al., *J Neuroscience* 2006). Together, P1 and P2 provide a new theory of motor planning. P3 revealed that, counter to the prevailing view, "low-level" movement features such as peak movement speed are planned in addition to "high-level" features (Churchland, Santhanam & Shenoy, *J Neurophysiology* 2006). In P4 we discovered that fluctuations (noise) in this planning process actually account for a great deal of variability during the upcoming movement (Churchland, Afshar & Shenoy, *Neuron* 2006}. Together, P3 and P4 have caused our group and others to begin revising the current theory of motor control. In P5 we demonstrated that planning occurs in neither an "intrinsic" nor an "extrinsic" reference frame (Churchland & Shenoy, *J Neurophysiology* 2007, in press), and P6 demonstrated that, surprisingly, eye position signals modulate arm movement planning signals (Batista et al., in review at *J Neurophysiology*). We also observed that planning activity often exhibits dynamics beyond that driven by external stimulation, presumably reflecting the extensive recurrence of neural circuitry. Characterizing these non-linear dynamics may reveal important features of neural computation. In P7, we have started to demonstrate that the

dynamics underlying PMd plan activity can be captured by a low-dimensional non-linear dynamical systems model, with underlying recurrent structure and stochastic point-process output (Yu et al., *NIPS* 2006).

2) How can we decode the desired prosthetic movement from neural signals?

We recently designed and validated two new algorithms for estimating reaching arm movements from neuronal ensemble activity, with the goal of increasing estimation performance and decreasing the amount of neural information required. In P8 we used a mathematical model of natural movement as a foundation for a decoding system (Kemere et al. *IEEE Transactions in Biomedical Engineering* 2004), and in P9 we developed a mixture-of-trajectory models framework (Yu et al., *J Neurophysiology* 2007), and found that both approaches can dramatically increase the accuracy of movement prediction.

3) What are the fundamental performance limits of communication prostheses?

We designed and demonstrated (P10), using electrode arrays implanted in monkey PMd, a four-fold higher performance brain-computer interface than previously reported (Santhanam et al., *Nature* 2006). This is, by a wide margin, the current world record and appears to be approaching fundamental neurobiological limits. This result helps motivate, and justify, the clinical use of such neural prosthetic systems. We also recently conducted studies to (P11) quantify how neurons are altering their response properties when "switching plans" at high speeds, to (P12) design and test algorithms to contend with these altered responses and restore high-accuracy estimates, to (P13) design and test algorithms to optimally place visual targets based on neural responses (Cuningham et al., *IEEE Engineering in Medicine and Biology* 2006), and to (P14) design and test algorithms to estimate cognitive state in real time (Achtman et al., in review at *J Neuroengineering*).

4) How can we design low-power circuits appropriate for surgical implantation?

Reducing power requirements has been a major focus of the medical device industry, and neural prostheses which require electronics close to the brain pose a significant challenge. In collaboration with Prof. R. Harrison (EE, U. Utah), we demonstrated analog low-power local field potential (P15) and threshold (P16) chips, and together with Prof. T. Meng (EE, Stanford) we demonstrated the feasibility of lower-power digital spike sorting chips (Zumsteg et al. IEEE *Transactions in Neural Systems and Rehabilitation Engineering* 2005, P17). Finally, we recently reported (O'Driscoll et al. *ISSCC* 2006) a novel low-power analog-to-digital converter which minimizes sampling resolution, and therefore power, while maintaining optimal prosthesis performance (P18).

5) How can we characterize bio-MEMs signals and design less-invasive alternatives?

Permanently implanted electrode arrays sense electrical signals from neurons close to their tips. Due to rapid head turns and immunological effects, electrodes move in relation to neurons and are not able to sense the same neurons for indefinite periods of time. To

make the first quantitative measurements of these electrode changes (P19), essential for enabling multi-day plasticity studies and adaptive signal processing algorithms for prostheses, we designed and built a miniaturized recording system (with Prof. T. Meng) and are now collecting, for the first time ever, neural and 3D accelerometer data from freely-behaving monkeys (Santhanam et al., *IEEE Transactions in Biomedical Engineering* 2007). Optical techniques may well provide longer lifetime neural sensors, by virtue of being less invasive than electrodes. In collaboration with Profs. J. Harris (EE, Stanford) and S. Smith (MCB, Stanford), we are currently designing a semiconductor optoelectronic brain-imaging chip and conducting proof-of-concept tests (Lee et al., *IEEE EMBS* 2006, P20). This technology should provide the first optical measurements from freely behaving animals, and will provide a new class of neural prosthetic control signals.

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